

IN THE SPECIFICATION:

Please amend the specification as shown:

Please delete paragraph [019] on page 6, and replace it with the following paragraph:

[019] **FIG. 1.** Comparison of deduced *D. melanogaster* cDNA SD07655 (**SEQ ID NO: 1**) and human MRP1 (**SEQ ID NO: 6**) amino acid sequences. The two amino acid sequences were aligned using ClustalW. Identical residues are marked with shading. The transmembrane regions are noted by a fine underline and the ATP-binding domains are noted by a bold underline. The amino acids derived from exons 4 and 8 of the dMRP gene are presented in bold characters. The small vertical lines above and below the amino acids denote the exon junctions with the type of splice junction marked by a number noting the class: 0, 1 or 2. The dMRP amino acid sequence differs from that of sequence AY069827 at the following positions : L/V pos. 124, M/L pos. 318 and I/T pos. 448.

Please delete paragraph [022] on pages 7-8, and replace it with the following paragraph:

[022] **FIG. 4.** Amino acid alignment of dMRP variable exon 4 (A) (**SEQ ID NOS 7 & 8**) and 8 (B) (**SEQ ID NOS 9-15**) encoded peptides with the cognate peptides from other organisms. The variant dMRP peptide sequence and the equivalent sequences

from *Drosophila* sulfonylurea receptor (Dsur, NG_000795) (**SEQ ID NOS 134 & 138**) and three human MRPs (MRP1, NM_004996 (**SEQ ID NOS 131 & 135**); MRP2, NP_005836 (**SEQ ID NOS 132 & 136**); and MRP3, Y17151 (**SEQ ID NOS 133 & 137**)) were aligned using ClustalW. Pfam (**SEQ ID NO: 139**) refers to pfam00664, a consensus sequence for ABC transporter Membrane Spanning Domains. Gaps were introduced to maximize sequence identity and are shown by a horizontal dash. Residues that are identical in at least half of the sequences have their background shaded and those present in more than half of the sequences are listed in the consensus (Cons). (C) Dendrogram constructed with the data of part (B) of the Figure (see *infra* for details).

Please delete paragraph [024] on page 8, and replace it with the following paragraph:

[024] **Fig. 6.** Comparison of deduced *A. gambiae* gMRP1a-d (**SEQ ID NOS 2-5**), *Drosophila melanogaster* dMRP (**SEQ ID NO: 1**), and human MRP1 (**SEQ ID NO: 6**) amino acid sequences. The alignment was produced using ClustalW. Identical residues in at least half of the sequences are marked with shading. The different topological regions are indicated in bold and italic above the sequences, and are delimited by vertical bars. *MSD1-3*, Membrane Spanning Domains 1 to 3; *L_o*, cytoplasmic loop; *NBD1-2*, Nucleotide Binding Domain, *Linker*, region linking the two halves of the protein. Walker A and Walker B are indicated as *A* and *B*, and their sequences are

marked in bold, as well as the signature (C) of ABC transporters. The vertical lines in bold inside the amino acid sequences denote the exon junctions. Where several genes shared the same site, this one was emphasized by a delimitating box.

Please delete paragraph [052] on pages 21-22, and replace it with the following paragraph:

[052] DNA (10 µg) was digested with either *Bam*HI or *Hind*III and the fragments were separated by electrophoresis on a 0.8% agarose gel. Following transfer to Hybond-N nylon membrane and fixation, hybridization was carried out at 65°C (in 1% BSA, 0.25 M NaH₂PO₄ pH 7.2, 1 mM EDTA, 150 µg/ml salmon sperm DNA) with a PCR-derived *dMRP* probe covering 378 bases (forward primer: GATCCGTTTATTTCTTGCCGC **(SEQ ID NO: 53)**; reverse primer: TCCAGGGCAGTGATTACCACT **(SEQ ID NO: 54)**). After hybridization, the blot was washed (in 40 mM NaH₂PO₄ pH 7.2, 1% SDS, and 1 mM EDTA) 1X at RT and 2X at 65 C°.

Please delete Table 3, on page 31, and replace it with the Table at Tab A.

Please delete Table 5, on page 39, and replace it with the Table at Tab B.



TABLE 3. Intron-exon organization of the *Drosophila* dMRP gene

| Exon | | 3' acceptor ^a (SEQ ID NOS 55- 72, respectively, in order of appearance) | | 5' donor (SEQ ID NOS 73- 90, respectively, in order of appearance) | | Intron | |
|------|-----------|---|-------|---|----|--------|-----------|
| n° | Size (bp) | n° | | n° | | Phase | Size (bp) |
| 1 | 181 | -127 | 54 | TTCTGG / gtgagt | 1 | 0 | 74 |
| 2 | 1512 | gaacag / AACGCA | 129 | ATTAAG / gtgagt | 2 | 0 | 135 |
| 3 | 138 | acatag / GTGCTC | 1776 | TTCCTG / gtaaga | 3 | 0 | 128 |
| 4a | 147 | acaaag / GTTTCC | 2042 | GCCGAG / gtacag | 4 | 0 | 146 |
| 4b | 147 | ttttag / GTTTCA | 2335 | GTGCAA / gtaagt | 5 | 0 | 800 |
| 5 | 85 | gaatag / ACGCAA | 3282 | CTAAAC / gtaaga | 6 | 1 | 62 |
| 6 | 820 | atacag / CCCATC | 3429 | TTCCAT / gtaagt | 7 | 2 | 67 |
| 7 | 371 | ttttag / CTCCTG | 4316 | GCCAAG / gtaagt | 8 | 1 | 904 |
| 8a | 221 | ttctag / TCGCGA | 5591 | TATATG / gtaatt | 9 | 0 | 336 |
| 8b | 221 | tcgaag / TTGTTA | 6148 | TTTGCG / gtaatt | 10 | 0 | 385 |
| 8c | 221 | ttccag / TTACCT | 6754 | TTTGCG / gtaaat | 11 | 0 | 525 |
| 8d | 221 | atgcag / TGCTAT | 7500 | TTCTGG / gtaaat | 12 | 0 | 691 |
| 8e | 224 | tcccag / GTGTGC | 8412 | TTTATG / gtattt | 13 | 0 | 4965 |
| 8f | 221 | agctag / GTCTTT | 13605 | TTTCAG / gtaatc | 14 | 0 | 1141 |
| 8g | 221 | tcgcag / GTTTCA | 14967 | TTTCAG / gtaatt | 15 | 0 | 340 |
| 9 | 218 | gggtag / GTTCTG | 15528 | AGATCG / gtatgt | 16 | 2 | 64 |
| 10 | 507 | cttcag / CTTTAT | 15810 | GTTTCAG / gtaagc | 17 | 2 | 59 |
| 11 | 382 | atttag / AATAAT | 16376 | ATTTCAG / gtgggt | 18 | 0 | 4791 |
| 12 | 393 | ctatag / AAAACC | 21549 | | | | |

Table 5. Organization of exon-intron junctions in the *gMRPs*

| Exon | | | | Intron | | | |
|-------|---|-----------------|---|--|------|-------|-----------|
| Name | Location on protein sequence ^a | Size (bp) | 3' acceptor ^b | 5' donor ^b | Name | Phase | Size (bp) |
| | | | (SEQ ID NOS | (SEQ ID NOS | | | |
| | | | 91-110, respectively, in order of appearance) | 111-130, respectively, in order of appearance) | | | |
| MRP1a | 1 | 165 | | CCCTTG/gtgaga | 1 | 0 | 83 |
| | 2 | 234 | gtacag/GTGGAC | TCCTTG/gtaagc | 2 | 0 | 202 |
| | 3 | 566 | cttcag/GTGGGC | GCTGAG/gtaagt | 3 | 2 | 224 |
| | 4 | 3638 | atatag/ATTACT | | | | |
| MRP1b | 1 | ND ^c | | TTTTGG/gtaagt | 1 | 0 | 603 |
| | 2 | 300 | ttacag/GACGAT | GCTTAT/gtaagt | 2 | 0 | 76 |
| | 3 | 2144 | tttcag/ATTATG | ATACCA/gtaagt | 3 | 2 | 63 |
| | 4 | 804 | ctctag/GGAACT | CTTCAG/gtatgt | 4 | 2 | 73 |
| | 5 | 1315 | ttccag/AATTGT | ATTCAG/gtaaga | 5 | 0 | 65 |
| | 6 | 1441 | acacag/AAAACA | | | | |
| MRP1c | 1 | 418 | | GCTTAT/gtgagt | 1 | 0 | 69 |
| | 2 | 662 | atttag/ATCGAC | GATGCA/gtaagt | 2 | 2 | 96 |
| | 3 | 1497 | ttatag/AGAACT | TTATCA/gtaagt | 3 | 2 | 61 |
| | 4 | 77 | ttttag/GGAACT | ATGAAG/gtaagt | 4 | 1 | 60 |
| | 5 | 1369 | tttcag/AAATAT | CTTCAG/gttagt | 5 | 2 | 63 |
| | 6 | 382 | atctag/AATTGT | ATTCAG/gtgaga | 6 | 0 | 71 |
| | 7 | 293 | ttacag/AAAACA | | | | |
| MRP1d | 1 | ND ^c | | GCTTAT/gtgagt | 1 | 0 | 69 |
| | 2 | 662 | atttag/ATCGAC | CATGCA/gtacgt | 2 | 2 | 110 |
| | 3 | 1497 | tgcag/AGAAAT | ATACCA/gtgagt | 3 | 2 | 65 |
| | 4 | 80 | tttcag/ACAACT | AAGACG/gtaggt | 4 | 1 | 98 |
| | 5 | 1372 | caccag/AAATTA | CTTCAG/gtatct | 5 | 2 | 73 |
| | 6 | 382 | ttccag/AATTGT | ATTCAG/gtaaga | 6 | 0 | 65 |
| | 7 | 363 | ccacag/AAAACA | | | | |

a) The numbering is based on amino acid one being the putative first Met.

b) Capital letters are used for the sequence in the exon and small case letters for sequence in the intron.

c) Not Determined.